의학석사 학위논문

광범위 관내 상피암 성분을 동반한 유방암 크기 측정에서 유방 촬영술, 초음파 및 자기공명영상의 정확도

The accuracy of mammography, US, and MRI for measuring the size of invasive breast cancer with extensive intraductal component

울산대학교 대학원
의학과
김영은

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지도교수 차주희

이 논문을 의학석사학위 논문으로 제출함

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울산대학교 대학원
의학과
김영은

김영은의 의학석사학위 논문을 인준함

심사위원 김 학 희 인
심사위원 차 주 희 인
심사위원 채 은 영 인

울산대학교 대학원
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국문요약

연구제목: 광범위 관내 상피암 성분을 동반한 유방암 크기 측정에서 유방 촬영술, 초음파 및 자기공명영상의 정확도

연구배경: 침윤성 유방암에서 광범위 관내 상피암 성분 (EIC) 을 동반한 경우 유방 보존 수술 후 높은 국소 재발률과 연관이 있다. 이 연구에서는 EIC를 가진 유방암의 크기를 유방 촬영술, 초음파, 자기공명영상에서 얼마나 정확하게 측정할 수 있는지 비교하고자 한다.

연구방법: 2007년에서 2012년 사이 서울아산병원에서 유방암으로 수술 받은 6816명의 환자를 후향적으로 분석하였다. 광범위 관내 상피암 성분을 동반한 유방암 환자들 중 병리적으로 침윤성 유방암과 관내 상피암 성분의 크기가 각각 측정된 환자들 중 유방 촬영술, 초음파와 자기공명영상을 모두 촬영한 370명을 대상으로 각각의 영상에서 병변의 크기를 측정했다. 수술적으로 얻은 병리 결과의 크기를 기준으로 각 영상에서 측정된 크기의 상관 관계를 평가했다.

연구결과: 스피어먼 상관 계수 (Spearman's correlation coefficient)를 통한 분석에서 자기공명영상 (r=0.741)에서 병변의 크기는 EIC의 병리적 크기와 좋은 상관 관계를 보였고 유방 촬영술 (r= 0.661)과 초음파 (r=0.514)에서 병변의 크기는 EIC의 병리적 크기와 중등도의 상관 관계를 보였다. 급간내 상관계수 (ICC)를 통한 분석에서 자기공명영상의 종괴(ICC=0.672) 혹은 비종괴(ICC=0.612) 병변의 크기는 EIC의 크기와 좋은 상관 관계를 보였다. 또한 미세석회화가 없는 병변의 크기는 유방 촬영술 (ICC=0.620) 보다 자기공명영상 (ICC=0.796) 에서 EIC 크기와 더 높은 상관관계를 보였다. 하지만 미세석회화가 동반된 병변의 크기는

자기공명영상 (ICC=0.680) 이나 초음파 (ICC=0.532)에서 보다 유방 촬영술 (ICC=0.702)에서 EIC 크기와 더 높은 상관관계를 보였다.

연구결론: 수술 전 유방 촬영술, 초음파, 자기공명영상에서 측정된 병변의 크기는 관내 상피암 성분의 크기를 잘 반영하였다. 자기공명 영상은 유방 촬영술과 초음파에 비해 더 높은 상관 관계를 보였다. 하지만 유방 촬영술에서 미세 석회화를 동반한 병변은 자기공명영상이나 초음파에서보다 관내 상피암 성분의 크기를 더 정확히 평가하였다.

목차

표 및 그림 차례

서론

The gold standard of treatment for early invasive breast cancer is the breast-conserving surgery (BCS). The presence of extensive intraductal component (EIC) is considered as independent risk factor for local recurrence after BCS. Therefore, radiologic evaluation of tumor size with EIC is important for preoperative assessment.

The purpose of this study is to compare the accuracy of mammography, ultrasonography (US) and magnetic resonance imaging (MRI) for measuring the size of invasive breast cancer with EIC.

연구대상 및 연구방법

Study population

This retrospective study was approved by the institutional review board of our institution and requirement for informed consent was waived.

Between 2007 and 2012, we collected 6816 patients who underwent surgery for invasive breast cancer at our institution. Among them, women who had received neoadjuvant chemotherapy or who had previous breast surgery were excluded. The inclusion criteria were as follows: 1) the postoperative pathologic report of tumor presented EIC positive breast cancers, 2) the postoperative pathologic report of tumor which the size of invasive tumor and EIC was measured respectively, 3) the patients underwent all three of the preoperative mammography, ultrasonography (US) and magnetic resonance imaging (MRI). Among 1,800 women with EIC positive breast cancers, 707 women who had the pathology report which the size of invasive tumor and EIC was measured separately were identified. Finally, we included 370 women (age range, 27–76 years; mean age, 47 years).

Preoperative Evaluation and Imaging with Mammography, US, and MRI

Patients underwent preoperative mammography by using a full-field digital mammography system (Senographe DS; GE Healthcare, Milwaukee, Wis). US was performed by radiologists with a 14–16-MHz and 50-mm linear array transducer (IU 22; Philips Medical Systems, Bothell, Wash).

MRI Patients underwent dynamic contrast material–enhanced MRI with either a 1.5-T or 3.0-T system (Magnetom Avanto or Skyra, Siemens Medical Solutions, Erlangen, Germany; Achieva, Philips Medical Systems, Best, the Netherlands) using a dedicated breast coil. Before scanning, venous access was established in the anterior cubital vein. The patients were imaged in the prone position. Imaging protocols included a T2-weighted sequence and a dynamic contrast-enhanced fat-suppressed axial three-dimensional T1-weighted sequence that consisted of unenhanced and five contrast-enhanced acquisitions. The six dynamic sequences were performed before and after IV injection of the contrast material (0.2 mL/kg body weight gadopentate dimeglumine [Magnevist; Schering, Berlin, Germany] or 0.1 mmol/kg gadoterate meglumine [Dotarem; Guerbet, Villapinte, France]) using an MR imaging–compatible power injector (Spectris; Medrad, Pittsburgh, Pa) with a flow rate of 1 or 2 mL/sec followed by a 20-mL saline flush. Postprocessing manipulations included the production of standard subtraction and maximum-intensity projection (MIP) images.

Radiologic and pathologic interpretation

Two radiologists retrospectively reviewed in consensus the preoperative mammography, US, and MRI images and measured the extent of lesion, without any knowledge of the final histological results (Y.E.K and J.H.C., with 2 and 20 years of experience, respectively, specializing in breast imaging). All of the images were assessed according to the guidelines of the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS), 5th edition. We measured the largest diameter including the mass and any surrounding abnormalities on each of three imaging modalities. The lesion size of mammography was measured on images. The lesion size of US was referred to the report and measured on images, if measurement of tumor size was needed. The lesion size of MRI was measured on MIP reconstruction [1].

Also we categorized the type of lesion on each of three imaging modalities for statistical analysis as follow: on mammography, 1) mass or asymmetry only, 2) calcifications only, 3) calcifications around the mass or asymmetry, on US, 1) mass, 2) non-mass lesion, 3) mass and non-mass lesion, with associated findings such as a satellite nodule within 2 cm of the main tumor, duct extension, a ductal dilatation adjacent to the main mass with or without intraductal lesions, and echogenic foci, on MRI, 1) mass, 2) non-mass enhancement, 3) mass with non-mass enhancement.

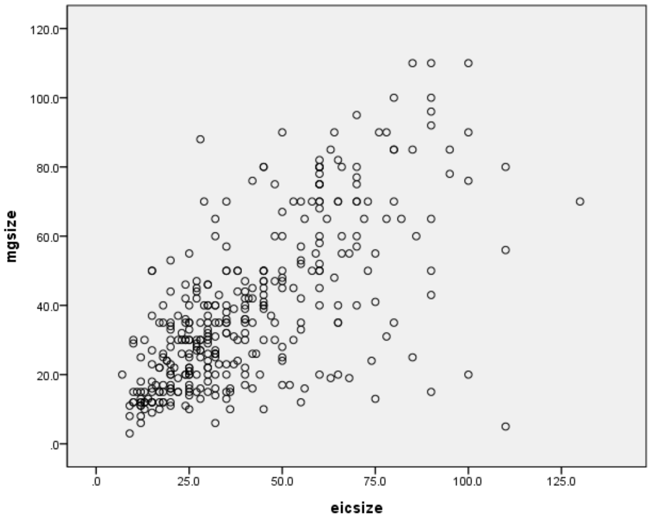
All pathologic specimens were obtained by definitive surgery. At pathologic examination, the maximum diameter of all malignant lesions, including the invasive cancer and EIC, was reported. The extent of ductal carcinoma in situ (DCIS) was evaluated by the dedicated breast pathologist. Schnitt et al. [2, 3] defined EIC as prominent DCIS within the invasive tumor occupying > 25% of the tumor and DCIS in the grossly normal adjacent breast tissue.

Statistical analysis

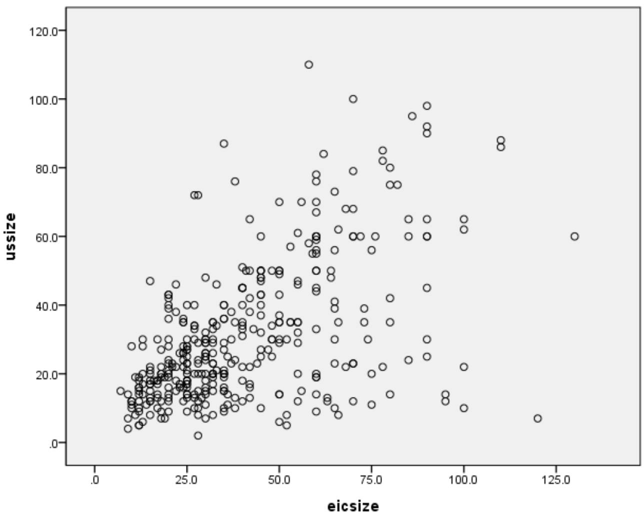
The statistical analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Spearman's correlation coefficient was used to analyze associations between radiologic tumor size and pathologic size of EIC. Spearman's correlation was interpreted as follow: coefficient >0.9 'excellent', coefficient 0.7–0.9 'good' and coefficient 0.5–0.7 'moderate'[4]. The intra-class correlation coefficient (ICC) was calculated to compare the agreement between the tumor size of subgroup on each image modalities and pathologic size of EIC. The ICC was interpreted as follow: ICC < 0.4, poor reliability; ICC, 0.4–0.59, fair reliability; 0.6–0.75, good reliability; ICC > 0.75, excellent reliability [5]. P values below 0.05 were considered significant.

연구결과

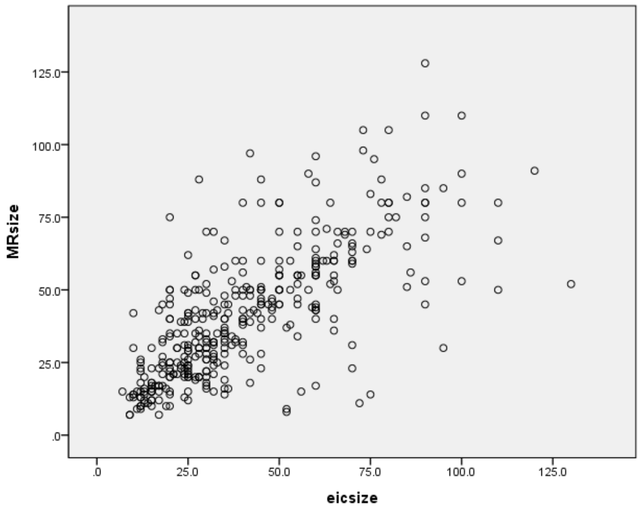
A total of 181 patients underwent mastectomy and 189 patients were treated by BCS. The mean size of EIC at pathology was 41.07 mm (range 7-130mm). The mean size of the lesion in mammography, US and MRI was 38.71 mm, 31.36 mm and 41.57 mm, respectively. Spearman's correlation coefficient was good between the size of lesion in MRI ($r=0.741$, $P < 0.001$) and EIC. The moderate Spearman's correlation was shown between EIC and the size of lesion in mammography ($r= 0.661$, $P < 0.001$) or US ($r=0.514$, $P < 0.001$) (figure1).



(A)



(B)



(C)

Figure 1. Scatterplot illustrating relationship between (A) the size of lesion in mammography and EIC (r= 0.661, $P < 0.001$), (B) the size of lesion in US and EIC (r= 0.514, $P < 0.001$), (C) the size of lesion in MRI and EIC (r= 0.741, $P < 0.001$).

The 345 EIC positive breast cancers of the 370 patients were categorized for the subgroup analysis by the type of lesion on each of three imaging modalities, because 21 lesions (0.06 %) were not visible in mammography and four lesions (0.01 %) were not visible in US. Table 1 summarizes the correlation between the size of EIC and lesion in subgroup of each modality.

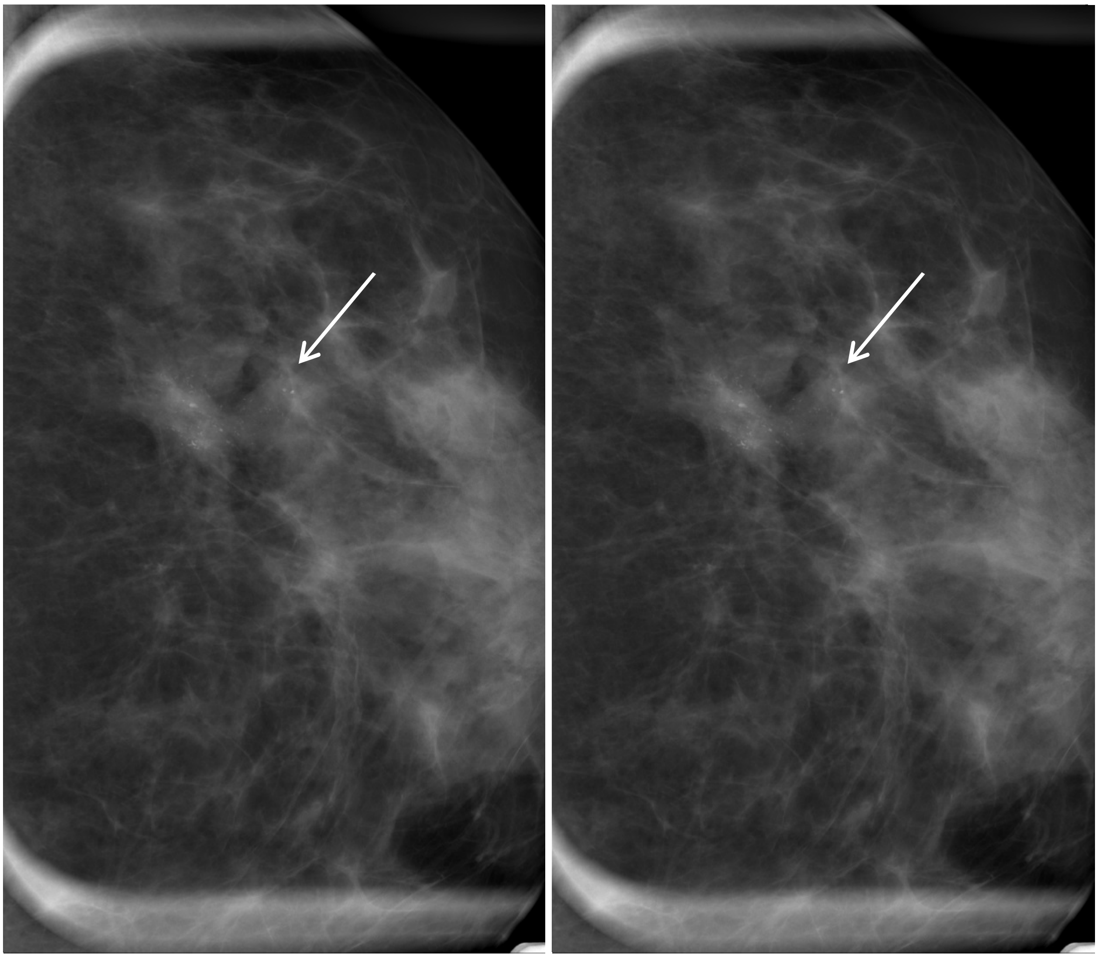
The most common mammographic feature of the EIC positive invasive cancer was calcifications within the mass (27.3 %; 101/370), followed by mass without calcification (22.2 %; 82/370), calcifications only (20 %; 74/370), calcifications around the mass (19.7 %; 73/370), and asymmetry (0.05 %; 19/370). The subgroup with calcifications of mammography shows better correlation between the size of lesion in mammography (ICC=0.702) and EIC (figure 2), compared with MRI (ICC=0.680) or US (ICC=0.532). The mean size of the subgroup with calcifications in mammography was 42.75 mm and the mean size of their EIC was 42.13 mm. However, the subgroup without calcifications of mammography shows better correlation between the size of lesion in MRI (ICC=0.796) and EIC than mammography (ICC=0.620). The mean size of the subgroup without calcifications in mammography and MRI was 28.77 mm and 38.06 mm respectively, with the 37.52 mm sized EIC.

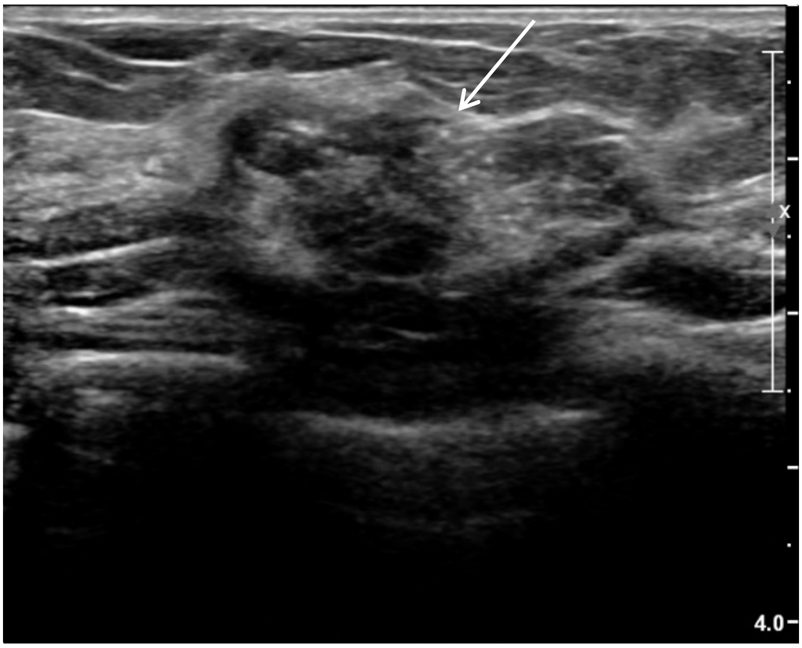
The most common US feature of the EIC positive invasive cancer was mass (69.2 %; 256/370), followed by nonmass (17 %; 63/370), and mass with nonmass (12.7 %; 47/370). The most common associated finding was echogenic foci with calcifications (47.3 %; 175/370). Other associated findings of ultrasound were a satellite nodule within 2 cm of the main tumor (24.3 %; 90/370), duct extension (0.08 %; 29/370) and a ductal dilatation adjacent to the main mass with or without intraductal lesions (0.06 %; 22/370). Also, all of above three associated findings were found in 45 lesions of 370 patients (12.2 %). The size of lesion with mass in US had poor correlation (ICC=0.287) with the size of EIC compared with mammography (ICC=0.624) and MRI (ICC=0.667). The mean size of mass in US was 24.48 mm and the mean size of EIC was 36.14 mm. The size of nonmass lesion with or without mass in US had good correlation (ICC=0.637) with the size of EIC, but showed lower correlation than mammography (ICC=0.651) and MRI (ICC=0.703). The mean size of nonmass lesion with or without mass in US was 48.29 mm and the mean size of EIC was 52.07 mm.

The most common MRI feature of the EIC positive invasive cancer was mass (50 %; 185/370), followed by nonmass (32.4 %; 120/370), and mass with nonmass (17 %; 63/370). The size of mass in MRI had good correlation (ICC=0.672) with the size of EIC, compared with mammography (ICC=0.658) and US (ICC=0.455). The mean size of mass in MRI was 29.16 mm and the mean size of EIC was 31.57 mm. The size of nonmass lesion with or without mass in MRI had good correlation (ICC=0.612) with the size of EIC, compared with mammography (ICC=0.6) and US (ICC=0.461). The mean size of nonmass lesion with or without mass in MRI was 54.89 mm and the mean size of EIC was 50.49 mm.

Table 1. ICC(Intraclass Correlation Coefficient) between the size of lesion in image and EIC

Subgroup analysis		**variables**	**ICC**
Mammography			
- Lesion without calcifications	EIC size	Size in mammography	0.620
		Size in ultrasonography	0.453
		Size in MRI	0.796
- Lesion with calcifications	EIC size	Size in mammography	0.702
		Size in ultrasonography	0.532
		Size in MRI	0.680
Ultrasonography			
- Mass	EIC size	Size in mammography	0.624
		Size in ultrasonography	0.287
		Size in MRI	0.667
- Nonmass or mass with nonmass	EIC size	Size in mammography	0.651
		Size in ultrasonography	0.637
		Size in MRI	0.703
MRI			
- Mass	EIC size	Size in mammography	0.658
		Size in ultrasonography	0.455
		Size in MRI	0.672
- Nonmass or mass with nonmass	EIC size	Size in mammography	0.600
		Size in ultrasonography	0.461
		Size in MRI	0.612

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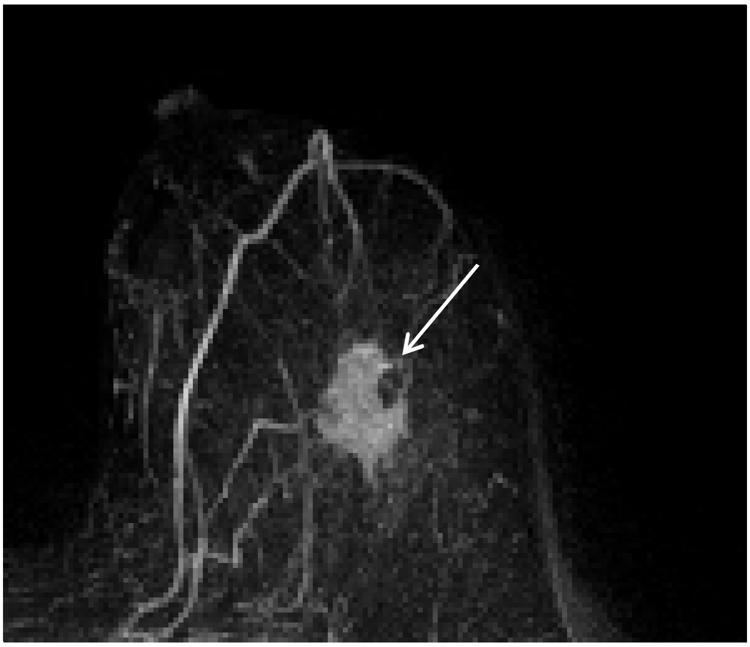

Figure 2. Images of an invasive breast cancer with an extensive intraductal component (EIC) of 80% in the left breast of a 55-year-old woman. The size of pathologic invasive tumor with EIC was about 36mm. (A, B) Mammography shows about 30mm sized indistinct and oval mass with grouped pleomorphic microcalcifications (arrow) in the left breast, (C) Ultrasonography shows about 26mm sized microlobulated hypoechoic mass(arrow) with microcalficiations in the left breast, (D) MIP image at preoperative MRI shows about 23mm sized irregular heterogeneous enhancing mass (arrow) in the left breast.

고찰

The BCS is the gold standard of treatment for invasive breast cancer, with the goal of achieving clear resection margins and complete excision of malignant foci [6]. The preoperative identification of EIC is important, because the presence of EIC is a significant and independent risk factor for postoperative local recurrence of breast cancer [7]. Therefore, accurate preoperative measurement of the invasive cancer and DCIS by imaging is obligatory in therapy planning of breast cancer [8]. Recently multiple studies have been published which are assessing the correlation between various imaging modalities and pathologic tumor size [8, 9]. Furthermore, several studies investigate the variable imaging features of EIC positive breast cancer [10-12]. However, there are a few published articles about the radiologic and pathologic correlation of the size of EIC. We found that the size of lesion on mammography, US, and MRI shows significant correlation with the extent of the EIC of invasive breast cancer.

According to our results, the mammography of invasive cancer with calcifications provides the most accurate extent of EIC. In previous studies, the EIC positive cancer show more likely to have suspicious calcifications at mammography than invasive cancer without EIC [10, 13]. Similar to our study, the previous study about the performance of mammography to detect EIC suggested that preoperative mammography showed good performance with the feature of suspicious calcification with or without a mass [14]. Furthermore, Stomper et al reported that the calcifications with greater than 3 cm in extent are more likely to have an EIC [13]. Likewise, our study shows larger mean size of the subgroup with calcifications in mammography than subgroup without calcifications.

In our study, US shows poor correlation with the pathologic size of EIC, especially the subgroup of mass. The sensitivity of detecting EIC by US varies widely [11, 15], but the results from the recent study demonstrated that US showed lower performance than mammography and MRI [14]. A number of US factors influence on these results. The major limitation of US is low capability to visualize microcalcifications [16]. Similar to our study, some associated findings of US are commonly found in EIC positive cancers such as satellite nodules, duct extension, long ductal dilatation adjacent to the tumor, or calcification [10, 17]. These associated findings should be detected and measured to consider the extent of EIC.

In previous studies, the presence of malignant nonmass enhancement with or without mass in MRI is significantly correlated with EIC positive breast cancer and associated with a positive resection margin [18, 19]. Results of our study additionally suggest that the size of both mass and nonmass lesion has good correlation with the size of EIC. In our study, MRI shows good correlation with size of EIC in subgroup without calcifications in mammography. Some previous studies of US and MRI suggested that EIC positive cancer showed linear continuous or segmental enhancement from the main tumor to the nipple in MRI and ductal dilatation in US correlated with linear, regional, or segmental enhancement in MRI [12, 20]. Similar to our study, a previous study suggested that mammography and US had a tendency to underestimate and MRI showed overestimate foci [21].

There were several limitations to this study. First, it was a retrospective analysis and we had a limited number of patients from a single institution, which potentially limits the general applicability of our findings. Second, we had to rely on pathologic reports, without re-analysis of the surgical specimens. Third, we also did not valuate inter-observer variability in the analysis of imaging features. Lastly, US imaging analysis was based on static images and real-time evaluation was not possible.

결론

In conclusion, the size of lesion on mammography, US, and MRI can reflect the preoperative size of the EIC of invasive breast cancer. MRI shows higher correlation with EIC than mammography and US. However, cancer with microcalcifications of mammography shows more accurate size of EIC than MRI or US. Therefore, radiologists should carefully evaluate the lesions in mammography, US, and MRI with associated findings to avoid underestimate the size of EIC.

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영문요약

The accuracy of mammography, US, and MRI for measuring the size of invasive breast cancer with extensive intraductal component

Author: Young-eun Kim, MD. Department of Radiology and the Research Institute of Radiology, Seoul Medical Center.

Background: To compare the accuracy of mammography, US and MRI for measuring the size of invasive breast cancer with extensive intraductal component(EIC).

Methods: Between 2007 and 2012, we collected 6816 patients who underwent surgery for invasive breast cancer at our institution. We reviewed the postoperative pathologic report of tumor which the size of invasive tumor and EIC was measured separately. Finally, we included 370 women diagnosed as invasive breast cancer with EIC, who underwent all three of the preoperative mammography, US and MRI. Each modality was retrospectively reviewed to evaluate the size of cancer with EIC. The reference standard was surgical pathologic findings. The accuracy of the imaging and pathologic features was evaluated.

Results: Spearman's correlation coefficient was good between MRI (r=0.741) and EIC, and moderate between mammography (r= 0.661) or US (r=0.514) and EIC. The lesion with mass or nonmass had good correlation (ICC =0.672 and 0.612 respectively) between MRI and EIC. Furthermore, the subgroup without microcalcifications shows higher correlation between MRI (ICC=0.796) than mammography (ICC=0.620). However, the subgroup with microcalcifications shows good correlation between mammography (ICC=0.702) and EIC, compared with MRI (ICC=0.680) or US (ICC=0.532).

Conclusions: The size of lesion on mammography, US, and MRI can reflect the preoperative size of the EIC of invasive breast cancer. MRI shows higher correlation with EIC than mammography and US. However, cancer with microcalcifications of mammography shows more accurate size of EIC than MRI or US.
Keywords: Extensive intraductal component, Mammography, MR imaging, Ultrasound